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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/350,518	07/09/1999	JOHN C. REED	066654-0515	8259
20583 JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			EXAMINER SANG, HONG	
			ART UNIT 1643	PAPER NUMBER
			MAIL DATE 04/21/2011	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

09/350,518

**Applicant(s)**

REED, JOHN C.

**Examiner**

HONG SANG

**Art Unit**

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 November 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81 and 83-109 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81 and 83-109 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-943)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

**RE: Reed**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/16/2010 has been entered.

2. Claims 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81, and 83-109 are pending. Claims 1-10, 13-15, 17-21, 28-31, 35-43, 45-49, 55, 57, 70-72 and 82 have been cancelled. No claims have been amended.

3. Claims 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81, and 83-109 are under examination.

### ***Rejections Maintained***

#### ***Claim Rejections - 35 USC § 102***

4. The rejection of claims 11, 16, 24, 25, 27, 32, 34, 44, 50-54, 56, 58-61, 67, 68, 75, 76, 78, 79, 81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98, and 100-109 under 35 U.S.C. 102(b) as being anticipated by Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print), as evidenced by Krajewski et al. (Endocrine-

Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

It is noted that the rejection of claims 26 and 77 is withdrawn upon further consideration.

Applicant presented the same arguments as before, and these arguments have been fully responded in the previous office action mailed on 6/17/2010. The rejection is maintained for the reasons of record.

***Claim Rejections - 35 USC § 103***

5. The rejection of claims 11, 12, 16, 24, 25, 27, 32-34, 44, 50-54, 56, 58-61, 67-69, 75, 76, 78-81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98, and 100-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Sano et al. (US patent NO. 5665539), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

It is noted that the rejection of claims 26 and 77 is withdrawn upon further consideration.

See paragraph 10 below for response to arguments.

6. The rejection of claims 11, 16, 24, 25, 27, 32, 34, 44, 50-54, 56, 58-68, 75, 76, 78, 79, 81, and 83-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Sauter

et al. (British Journal of Cancer, 1997, 76(4): 494-501), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

It is noted that the rejection of claims 26 and 77 is withdrawn upon further consideration.

See paragraph 10 below for response to arguments.

7. The rejection of claims 11, 16, 24, 25, 27, 32, 34, 44, 50-54, 56, 58-68, 75, 76, 78, 79, 81, and 83-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Love (US Patent No. 6,221,622B1, Date of Patent 4/24/2001, earliest effective filing date 4/28/1998), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

It is noted that the rejection of claims 26 and 77 is withdrawn upon further consideration.

See paragraph 10 below for response to arguments.

8. The rejection of claims 11, 16, 22-27, 32, 34, 44, 50-54, 56, 58-61, 67, 68, 73-79, 81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98, and 100-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print), in view of Mather et al. (Clin. Cancer Res., 1998, Aug., 4:1851-1856), and McGuire et al. (US 5,188,964, Date of Patent: 2/23/1993), as evidenced by

Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

See paragraph 10 below for response to arguments.

9. The rejection of claims 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81, and 83-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print), in view of Mather et al. (Clin. Cancer Res., 1998, Aug., 4:1851-1856), McGuire et al. (US 5,188,964, Date of Patent: 2/23/1993), Sano et al. (US patent NO. 5665539), and Love (US Patent No. 6,221,622B1, Date of Patent 4/24/2001, earliest effective filing date 4/28/1998) is maintained.

See paragraph 10 below for response to arguments.

***Response to Applicant's arguments to 103(a) rejections***

10. The response states that the breast cancer disclosed by Turner encompasses breast cancer at stage I, II, III and IV. Turner et al., alone or in combination with cited references, do not teach, expressly or inherently, the claimed methods relating to stage I or stage II of breast cancer. Turner et al. describe a retrospective study that showed no statistically significant correlation ( $p=0.06$ ) between invasive carcinoma patient's survival and overexpression of cytoplasmic BAG-1. One skilled artisan would have understood that this relatively small differential in overall survival rate is not significant enough to conclusively suggest that BAG-1 can be a reliable diagnostic tool for

predicting survival, let alone being a diagnostic tool for predicting survival of patients with stage I or stage II of breast cancer as claimed. The disclosure of Turner et al. as evidenced by Krajewski et al., actually teaches away from the claimed methods. At best, Krajewski et al. disclose higher levels of BAG-1 nuclear immunostaining (>20%) correlated with longer OS among patients with early stage breast cancer ( $p0.001$ ) (see page 36, first column, lines 19-23). In view of the disclosure of Turner et al. that there was no statistically significant correlation between OS and DDFS for invasive carcinoma patients with overexpression of cytoplasmic BAG-1, and the disclosure of Krajewski et al. that higher levels of BAG-1 nuclear immunostaining correlated with OS among patients with early stage breast cancer, one skilled in the art would not have had a reasonable expectation of success in practicing the claimed methods.

Applicant's arguments have been carefully considered but are not persuasive. Applicant's arguments of p value are not persuasive because p value is not a standard for determining the obviousness. The standard is whether the combination of the cited references teaches every limitation of the claims and whether there is a motivation and reasonable expectation of success to combine the teachings of the cited reference to arrive the claimed methods. Although Turner's reference discloses retrospective study, the method steps taught by Turner are the same as the instant claims. The claims as written do not differentiate the claimed method from a prior art method. Due to variation of the size of patient population to be analyzed and variation of sample preparation, grading and classification, one method is more likely to give different results (p values). Applicant's arguments of teaching away are not persuasive because detection of the

level of cytoplasmic BAG-1 in breast cancer tissue and further correlation of the level with the patient survival were explicitly taught by Turner, the primary reference (a single reference), therefore no motivation to combine with other cited references to detect cytoplasmic BAG-1 does not apply in this situation. With respect to stage I and II breast cancer, the invasive carcinoma disclosed in Turner's reference is in fact an early stage invasive breast cancer which includes stage I and stage II breast cancer, as evidenced by Krajewski and Exhibit II (see also previous office action mailed on 6/17/2010). Furthermore, both Maher and McGuire et al. teach that there is a great need for a general method of predicting tumor recurrence in early stage breast cancer patients. Given the teachings of Turner that subcellular location of BAG-1 may have prognostic importance with respect to survival of breast cancer patients, one skilled in the art would have been motivated to use the method of Turner for predicting the disease-free or overall survival of early stage (stages I and/or II) breast cancer patients. One would have had a reasonable expectation of success because Turner et al. have shown that the 10-year overall survival (OS) and distant disease free survival (DDFS) for breast cancer patients with overexpression of cytoplasmic BAG-1 in IC specimens was 75% and 70%, respectively, compared to 62% and 35% for tumors with low cytoplasmic BAG-1 levels.

For the forgoing reasons, the rejection is maintained.

***New Grounds of Objections***



***Claim Objections***

11. Claims 73-75 are objected to for being dependent from a cancelled claim.

***Conclusion***

12. No claims are allowed.
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to HONG SANG whose telephone number is (571)272-8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.